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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1634	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/824,656	FRANZEN ET AL.	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-8 and 11-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-8, 11-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 4-8, 11-19 pending and examined on the merits.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/01/2007 has been entered.

This Office Action is in reply to Applicants' correspondence of 08/01/2007. Applicants' remarks and amendments have been fully and carefully considered but are not found to be sufficient to put this application in condition for allowance. New grounds of rejection presented in this Office Action are necessitated by Applicants' amendments. Any rejections or objections not reiterated herein have been withdrawn in light of the amendments to the claims or as discussed in this Office Action.

This Action is **NON-FINAL**.

Withdrawn Claim Rejections - 35 USC § 102

2. The rejection of claims 1, 4, 5, 7, 8, and 11 under 35 U.S.C. 102(b) as being anticipated by the teachings of Knoll (1999; WO 99/27367), as set forth in the previous office action, is **WITHDRAWN**.

The rejection of claims in view of the teachings of Knoll is withdrawn in light of the amendment to the claims to require a methods for measuring the binding of an analyte molecule to a probe in which a galvanic element formed and one of a current

and a voltage generated between the electrodes of the galvanic element is measured, where such methods are not taught by Knoll.

Applicants Remarks and Arguments of 08/01/2007 are largely drawn to the aspects of the instant claims that are not taught by Knoll, and are thus moot in view of the newly presented rejections set forth in this Office Action.

Withdrawn Claim Rejections - 35 USC § 103

3. The rejections of claims 5, 6, and 12-19 under 35 USC 103 as obvious in view of Knoll in view of: Henkens (claims 6, 18, and 19); Wohlstadter (claims 5 and 12); Fish (claims 13, 16, and17); Fish and Wohlstadter (claim 14); Fish, Wohlstadter, and Wang (claims 15) as set forth in the previous office action, are **WITHDRAWN**.

The rejections of claims in view of the teachings of Knoll, the primary reference required for all of the aforementioned obviousness rejections are withdrawn in light of the amendment to the claims to require a methods for measuring the binding of an analyte molecule to a probe in which a galvanic element formed and one of a current and a voltage generated between the electrodes of the galvanic element is measured, where such methods are not taught by Knoll.

Applicants Remarks and Arguments of 08/01/2007 are largely drawn to the aspects of the instant claims that are not taught by Knoll, and are thus moot in view of the newly presented rejections set forth in this Office Action.

New Claim Rejections - 35 USC § 103

4. Claims 1, 4, 7, 8, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (2001) (as cited on the PTO-892 of 10/10/2006), as evidenced by Town (1997) and Wang (1994; US Patent 5,292,423) in view of Knoll (1999; WO 99/27367)

Wang et al teaches a method for measuring the binding of a nucleic acid analyte molecule to a probe molecule.

Regarding claim 1, Wang et al teaches providing a circuit surface having a contact spot and a metal counterelectrode (Fig 1; p.5577 – Electrode preparation), relevant to part (a). Relevant to part (b) of claim 1, Wang et al teaches the immobilization of probe molecules (Fig 1; p.5777 – Preparation of oligomers coated microspheres and analytical procedure). Relevant to parts (c) and (d), Wang et al teaches binding streptavidin coated gold particles to the analyte molecules, and binding of the analyte molecules to the probe molecules (Fig 1; p.5578, left col., lns.5-11). Relevant to step (e), Wang et al teaches a counterelectrode that is Ag/AgCl and a nanoparticle surface that is gold, which are metals from an electrochemical series, and teaches analysis of the gold metal from the nanoparticle using potentiometer stripping analysis (PSA), where in PSA the gold is deposited on the contact spot of the circuit (which establishes electrical contact) and in the presence of an electrolyte a current producing galvanic element is formed (While Wang et al does not explicitly mention aspects of the PSA methodology relevant to the limitations of the claims (e.g. use of an electrolyte, and formation of a galvanic element), such elements are inherent to the PSA

metod as evidenced by Town (e.g.: p.407, left col., lns.14-30) and Wang (1994) (e.g.: col.1, lns.28-43)). Relevant to step (f), Wang et al teaches measuring the current generated between the electrodes in a PSA (Fig 3) and teaches that measurement in the PSA allows the biding of the analyte molecule to the probe to be measured (p.5579 – Analytical performance).

Regarding claim 8, Wang et al teaches that the gold nanoparticles are bound to the analyte after the analyte is bound to the capture probe (p.5578, left col., lns.8-11)

Wang et al does not teach probes immobilized in spatial proximity to the electronic circuits (as required by part (b) of claim 1), or probes immobilized on the circuit surface (claim 4) or a countersurface (claim 5). Wang et al does not teach a method in which nanoparticles are bound to analytes before the analytes are hybridized to the capture probe (claim 7), or methods where the electrical contact between the nanoparticle and the contact spot is established by electrically conductive molecules (claim 11).

Knoll et al teaches a method for electronic detection of the binding of analyte molecules to probe molecules. Relevant to step (b) of claim 1, Knoll teaches providing immobilized probe molecules in spatial proximity to a circuit surface having electronic circuits (see for example Fig 9 and 10).

Regarding claim 4, Knoll teaches probe molecules bound to the circuit surface (for example Fig 10).

Regarding claim 7, Knoll teaches the marker particle bound to the analyte prior to binding of an analyte to a probe (Fig 9), relevant to claim 7.

Relevant to claim 11, Knoll teaches that the marker particles may be conductive (col.14 lns.5-9), thus they are electrically conductive molecules.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the techniques of Knoll in the method for measuring the binding of analytes to probes as taught by Wang et al. One would have been motivated to use the methods of Knoll et al because Knoll et al teaches the successful deposition of conductive elements (termed 'marker particles by Knoll) using probes immobilized in spatial proximity to an electronic circuit of interest, and Wang et al teaches that such deposition is required (Fig 1) for the sensitive detection of analyte binding by using PSA (p.5578 – Chromopotentiometric stripping analysis).

Response to remarks

5. It is noted that the rejection set forth above is a new rejection which references the detection methodology of Wang et al (i.e. PSA) to render obvious the methods claimed in the instant application. While Wang et al has not previously been cited for its teachings of PSA detection methods, the reference has been previously applied to other aspects of the instant claims, and the teachings of Wang et al are addressed in Applicants Remarks of 08/01/2007 (P.9 of Remarks). Applicants have argued that the detection methods of Wang et al utilize electrochemical reactions at a working electrode and measuring electrical changes at the working electrode by potentiometeric means, not by forming a galvanic element and measuring the electrical properties of that element. This argument as it applies to the teachings of Wang et al has been

considered but is not found to be persuasive. The potentiometeric stripping analysis of Wang et al is a method in which the oxidation of gold (Au) to Au(III) generates a current between the electrodes of a circuit that is measured to detect the presence of the analyte (as evidenced by Wang (1994) and Town (1997). Thus, the measurement methods of Wang et al are applicable to the measurement methods of the instant claims.

6. Claims 6, 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (2001) (as cited on the PTO-892 of 10/10/2006), as evidenced by Town (1997) and Wang (1994; US Patent 5,292,423) in view of Knoll (1999; WO 99/27367) as applied to claims 1, 4, 7, 8, and 11 above, and further in view of Henkens et al (2002, US Patent 6,391,558).

The teachings of Wang et al, as evidenced by Town (1997) and Wang (1994) in view of Knoll are applied to claims 6, 18, and 19 as they were previously applied to claims1, 4, 7, 8, and 11.

Regarding claim 6, Knoll teaches probe molecules immobilized to an electrode surface, and analyte molecules affinity bound (e.g. antibody-antigen, Fig 5; DNA:DNA / probe:analyte hybridization) to the probe molecules, and Wang et al teaches biotin:avidin immobilization of a probe.

Wang et al in view of Knoll does not particularly require that the immobilized probe is bound by a covalent bond (claim 6), or provide any particular details regarding the binding of the nanoparticle to the analyte molecule (claims 18 and 19).

Henkens et al teaches methods for the detection of nucleic acids using electrodes comprising immobilized probes, as well as analyte molecules labeled with detectable reporters.

Regarding claim 6 Henkens et al specifically teaches that capture probes may be covalently bound to an electrode (col.45 lns.16-25).

Regarding claims 18 and 19, Henkens et al teaches the PCR amplification of a analyte DNA molecule using primers modified at the 5' end, and gives the examples of fluorescein and biotin labeled primers (col.21 ln.60 - col 22. ln.4). Henkens et al indicates that the resulting labeled PCR product may be attached to a reporter molecule by an interaction between the label from the PCR primer and a binding partner for the label of the primer. Relevant to claim 18, Henkens et al teaches the biotin:avidin binding pair, as well as labeling a PCR product using a biotinylated primer, and binding of the labeled PCR product to a avidin-gold biding partner (for example col.5 lns.25-35, col.43 ln.55). Relevant to claim 19, Henkens et al particularly teaches biding of a fluorescein-labeled PCR product to an anti-fluorescein HRP conjugate.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the nucleic acid probe immobilization methods of Henkens et al in the electrode based analysis methods of Wang et al in view of Knoll. One would have been motivated to do so based on the assertion of Henkens et al that covalent attachment of a probe is a preferred method (col.45 lns. 16-25). It would further have been obvious to use the probe:reporter binding method of Henkens et al to accomplish the marker particle:analyte binding of Wang et al in view of Knoll et

al. One would have been motivated to do so because Henkens et al teaches that such methods can be used to attach a variety of different molecules (including colloidal gold which is similar to the description of marker particles by Knoll) to nucleic acid for analysis.

7. Claims 5 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (2001) (as cited on the PTO-892 of 10/10/2006), as evidenced by Town (1997) and Wang (1994; US Patent 5,292,423) in view of Knoll (1999; WO 99/27367), as applied to claims 1, 4, 7, 8, and 11 above, and further in view of Wohlstadter et al (2001, US Patent 6,207,369).

As discussed in detail in the rejection of claims 1, 4, 7, 8, and 11 earlier in this Office Action, Wang et al in view of Knoll teaches all of the required limitations of claims 1 and 11, from which claims 5 and 12 depend.

Wang et al in view of Knoll does not specifically teach probe molecules bound to a countersurface positioned opposite the circuit surface (claim 5), or the use of polyene molecules to conduct an electrical signal (claim 12).

Regarding claim 5, Wohlstadter et al teaches methods of using several configurations of electrode-based devices in which the portion of the device where the analyte is collected (termed in the reference the 'binding domain') is on a surface opposite from an electrode (see for example Fig. 21 and Fig. 37).

Regarding claim 12, Wohlstadter et al teaches the use of a linking chain to ensure low resistance of electron transfer from the electrode, and specifically teaches the use of a polyacetylene chain (col.39 lns.53-63), which is on the polyene class.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have performed the electronic detection methods of Wang et al in view of Knoll using a probe binding area on a countersurface opposing an electrode. One would have been motivated to do so based on the teachings of Wohlstadter et al that in such a configuration the electrode can be protected during the binding reaction from the sample by a physical barrier that is subsequently removed thus, preventing contamination of the electrode surface which could result in a change in its electrochemical performance (col.64 lns.1-11). One would have a reasonable expectation of success because Wohlstadter et al teaches that the binding domain of the countersurface makes contact with the electrode and carries current from the counter electrode to the working electrode (col.45 lns.9-35). It would have been further obvious to use the polyacetlyene chains of Wohlstadter et al to ensure low resistance of conductivity from the electrode to the marker particle as Wohlstadter et al teaches this use for polyacetylene chains.

8. Claims 13, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (2001) (as cited on the PTO-892 of 10/10/2006), as evidenced by Town (1997) and Wang (1994; US Patent 5,292,423) in view of Knoll

(1999; WO 99/27367), as applied to claims 1,4, 7, 8, and 11 above, and further in view of Fish (2002, WO 02/054052 A1).

As discussed in detail in the rejection of claims 1, 4, 7, 8, and 11 earlier in this Office Action, Wang et al in view of Knoll teaches all of the required limitations of Claim 1, from which claims 6, 18 and 19 depend.

Relevant to claim 16, Knoll specifically teaches that the marker particles may be magnetic (see for example col.4 lns.10-24).

Relevant to claim 17, Knoll teaches that the marker particles may be dendrimers (col.14 lns.2-3), which are protrusions.

Wang et al Knoll does specifically teach a requirement of nanoparticles touching a contact spot, though Wang et al teaches the requirement of the nanoparticle element (i.e.: gold (Au)) contacting the electrode.

Fish teaches the detection of analytes using an electrode-based method wherein an opposing surface with an electrode is moved to make contact with an electrically readable particle that is bound to and analyte, where the analyte is bound to an immobilized probe (see for example Fig 1, p.14-18). Regarding claim 13, Fish specifically teaches that pressure is applied to the particle (p.16 last two lines) and that the bound particles make contact with the electrode (p.17 lns.7-8).

Regarding claim 16, Fish teaches that a countersurface may be moved in order to create a physical contact between an electrode (which is a contact spot) and an electrically readable particle, and also teaches that the probes may be attached to a

contact spot and that movement of the countersurface causes the particles to make contact with the contact spot (see for example Fig 13 and page 28).

Additionally relevant to claim 17, Fish teaches that an electrode may be rough and have sharp edges and vertices to make electrical contact (p.42), thus teaching a circuit surface with electrically conductive protrusions.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have performed the electrode-based analyte detection method of Wang et al in view of Knoll by incorporating the countersurface movement taught by Fish to make contact between a particle and an electrode. One would have been motivated to do so based on the teachings of Fish that such methods allow accurate electrochemistry to be performed quickly at a low cost (p.7), and the teaching of the methods of Wang et al requiring contact between the element of the nanoparticle and the electrode. One would have had a reasonable expectation of success because Wang et al in view of Knoll teaches that the electrode-based method can be used as a multi-step process separating the steps of particle transport and electrode binding (Knoll et al at col. 5 lns.62-67).

9. Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al (2001) (as cited on the PTO-892 of 10/10/2006), as evidenced by Town (1997) and Wang (1994; US Patent 5,292,423) in view of Knoll (1999; WO 99/27367) and Fish (2002, WO 02/054052 A1), as applied to claims 13, 16, and 17 above, and further in view of Wohlstadter et al (2001, US Patent 6,207,369).

The teachings of Wang et al in view of Knoll and Fish are applied to claim 14 as they were previously applied to claims 13, 16, and 17.

Wang et al in view of Knoll and Fish teaches an electrode-based method of analyte detection wherein marker particles bind to analyte molecules and contact between the marker particle and a contact spot is made by the nanoparticles touching the contact spot.

Regarding claim 15, Wang et al a method in which a gold nanoparticle binds to a target oligonucleotide wherein the target oligonucleotide has hybridized to a probe oligonucleotide immobilized to a solid support (Fig 1; p.5577, left col., lns.5-10). The method of Wang et al includes a step of dissolution of the gold nanoparticle from the analyte molecule prior to detection of the gold nanoparticle at an electrode.

Wang et al in view of Knoll and Fish does not specifically teach that the analyte molecule:particle complex is located on a surface opposite the circuit surface.

Wohlstadter et al teaches methods of using several configurations of electrode-based devices in which the portion of the device where the analyte is collected (termed in the reference the 'binding domain') is on a surface opposite from an electrode (see for example Fig. 21 and Fig. 37).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the opposed binding and electrode surfaces taught by Wohlstader et al in the electrode-based analyte detection method of Wang et al in view of Knoll and Fish. One would have been motivated to do so based on the teachings of Wohlstadter et al that in such a configuration the electrode can be

protected during the binding reaction from the sample by a physical barrier that is subsequently removed thus, preventing contamination of the electrode surface which could result in a change in its electrochemical performance (col.64 lns.1-11).

Conclusion

10. No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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